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Neighboring-Group Participation by C-2 Ether Functions in Glycosylations Directed by Nitrile Solvents

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Abstract: Ether-protecting functions at C-2 hydroxy groups have been found to play participating roles in glycosylations when the reactions are conducted in nitrile solvent mixtures. The participation mechanism is based on intramolecular interaction between the lone electron pair of the oxygen atom of the C-2 ether function and the nitrile molecule when they are positioned in a *cis* configuration. A 1,2-*cis* glycosyl oxazolinium intermediate is formed. This participation, in conjunction with the anomeric effect of the glycosyl donor, confers high 1,2-*trans* selectivities on glycosylations. Further application of this concept has led to efficient preparations of α-(1→5)-arabinan oligomers.

Keywords: arabinans · glycosylation · neighboring-group effects · nitrile solvents · oligosaccharides

Introduction

The use of protecting groups for regio- and stereochemical control is ubiquitous in organic synthesis.[1] Nowhere is this strategy more extensively exploited than in carbohydrate chemistry.[2–4] In a glycosylation, activation of the glycosyl donor produces a series of equilibrating oxocarbenium ion/counterion ion-pairs, such as the close-contact, solvent-separated, and free varieties. Such a notion was advocated by Winstein and later developed by Veron, Schuerch, and Lemieux (Figure 1a).[5,6] In the case of a glycosyl donor bearing an ester protecting function at the C-2 position, a dioxolenium ion is formed as a result of the dominance of the neighboring-group participation (NGP) effect, leading to exclusive 1,2-*trans* glycosidic bond formation (Figure 1b).[7,8] In the case of a donor bearing an ether-protecting function at the C-2 position, a mixture of α-and β-anomers is produced due to the absence of the NGP effect (Figure 1c). Accordingly, the C-2 ether-protecting group is also regarded as a nonparticipating function.[9]

In 2009 we reported a low-concentration β-selective glycosylation method (LCG) that enables the formation of 1,2-*trans* β-glycosidic bonds in CH_2Cl_2 and nitrile solvent mixtures (CH_2Cl_2/RCN) and the C-2 ester-participating function is thus not required.[10] In a carbohydrate context, the β-selectivity in glycosylation selectivity in a nitrile solvent is usually attributed to the formation of α-glycosyl nitrilium inter-

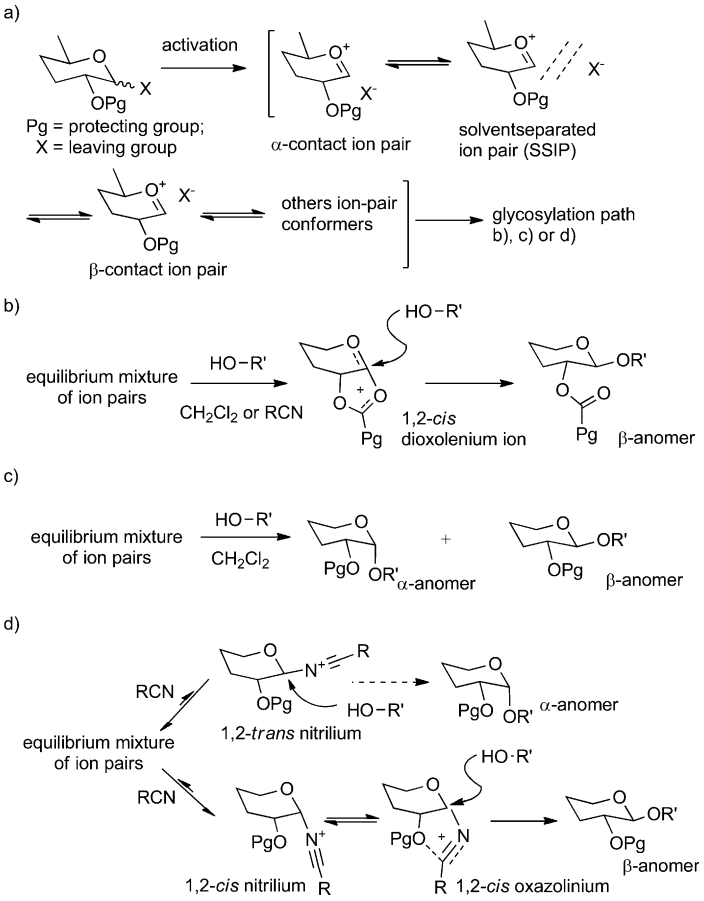

Figure 1. a) Activation of glycosyl donor. b) NGP glycosylation in CH_2CH_2 or nitrile solvent (RCN). c) Glycosylation with C-2 ether-function-protected donor in CH_2CH_2. d) Glycosylation with C-2 ether-function-protected donor in RCN.

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mediates.[11–13] Some evidence of the presence of such nitrilium species has emerged in the past. Hindsgaul, for example, applied an intramolecular trapping technique to detect the presence of nitrilium species,[14] whereas Crich reported the formation of an imidate side product on nucleophilic addition of an alcohol to the nitrilium species.[15] However, this mechanistic model is not sufficient to account for some observations from our LCG studies (see Results and Discussion). These studies revealed a structure–selectivity relationship between the configuration of the C-2 ether-protecting function and the selectivity of glycosylation in a CH_2Cl_2/RCN solvent mixture. These findings set off a series of investigations that demonstrated a previously unreported—to the best of our knowledge—participation role of the C-2 ether function in glycosylations when these reactions are conducted in CH_2Cl_2/RCN solvent mixtures.

Accordingly, a revised mechanism for glycosylations in nitrile solvents is proposed (Figure 1d). In this model, oxocarbenium ion/counterion ion-pairs interact with nitrile solvent molecules to produce mixtures of α- and β-glycosyl nitrilium intermediates. Because of the anomeric effect, the formation of the former α-nitrilium species is inherently favored, but this dominance is further promoted through the parcipitation of the oxygen atom in the C-2 ether function, which forms a glycosyl oxazolinium intermediate with the nitrile molecule. A prerequisite for such participation is a *cis* orientation of the ether function and the nitrile molecule. As a matter of fact, similar participation has been shown in nucleophilic additions of alcohols to acyclic alkyl nitriliums, but the alkyl nitrilium compounds are different stereoelectronically from glycosyl oxazolinium intermediates.[16] In the present context, because the α-face of the oxazolinium intermediate is blocked, the formation of a 1,2-*trans* β-glycosidic bond is forced when an acceptor is present. It should be noted that participation effects of other heteroatoms or aromatic systems have been demonstrated by a C-2 picolyl function in a thioglucosyl donor,[17] by *N*,*N*-dibenzylamine in a 2-amino-2-deoxy glycosyl donor,[18] by a C-2 thienylmethyl function in a glucosyl imidate,[19] and by a C-2 electron-rich anthracenyl ether-protecting function in glycosyl donors.[20] In addition, Turnbull also used density functional theory (DFT) to propose the formation of a furanosyl oxazolinium intermediate through remote participation by a C-5 thioether function.[21]

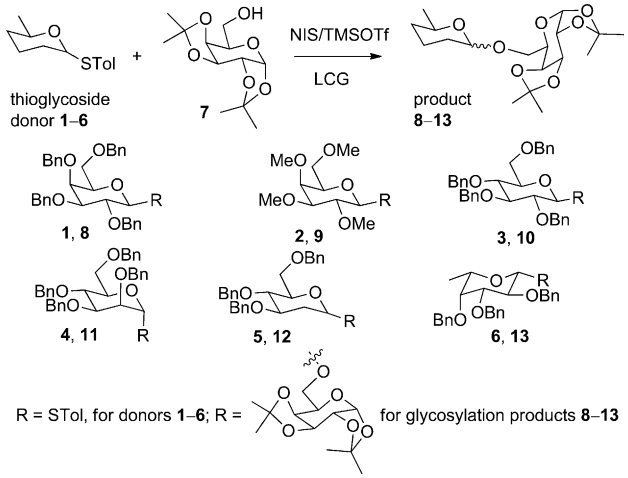
This paper reports an extended study of glycosylations under LCG conditions and reveals a participating role of the C-2 ether function. Elaboration of this participation concept has led to the development of an efficient 1,2-*trans* α-glycosylation method for thioarabinosyl donors, which has been found useful for the synthesis of α(1→5)-arabinan oligomers.

Results and Discussion

Stereoselectivity and configuration relationship: In an extension of a previous study, we examined the applicability of the LCG method to different thioglycosyl donors (**1**–**6**, Table 1).[22] For purposes of comparison, selected reactions were also carried out in CH_2Cl_2. Glycosylation of the galactosyl acceptor **7** with the thiogalactosides **1** and **2** and the thioglucoside **3** furnished the corresponding disaccharides **8**, **9**, and **10** in high yields and with excellent β-selectivities (Table 1, entries 1–3). These results show that a change in the configuration of the ether function at the C-4 position did not affect the glycosylation selectivity in a nitrile solvent. However, inversion of the configuration of the ether function at the C-2 position reversed the glycosylation selectivity, as illustrated by comparison of the results of glycosylations with the thioglucoside **3** and the thiomannoside **4** (Table 1, entries 3, 4).[12,23,24] Although the α-selective glycosylation observed for the thiomannoside **4** has been attributed to the reverse anomeric effect (RAE),[12,25] such a RAE hypothesis remains controversial in some cases.[26,27] We therefore interpreted the experimental data from a different perspective.

On examination of the glycosylation results and the structures of thioglycosides **1**–**4**, the C-2 ether function appears to exhibit a *trans*-directing property in nitrile solvents (Table 1, entries 1–4). This study verified this property by removing the substituent at the C-2 position in a glycosyl donor and ascertaining whether or not this donor still re-

Table 1. Extended LCG studies for the thioglycoside donors **1**–**6**.



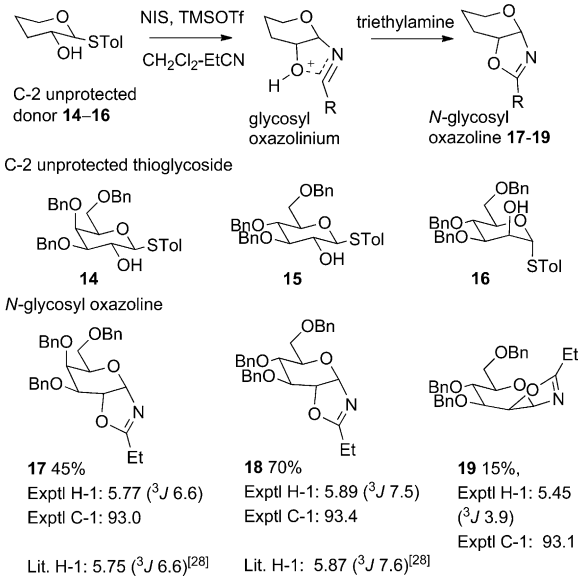
	Donor	Product	Yields [%]/α:β[a]	
			LCG[b]	CH_2Cl_2[c]
1	**1**	**8**	80/≈1:19	82/1:4
2	**2**	**9**	77/≈1:19	–
3	**3**	**10**	83/≈1:19	–
4	**4**	**11**	78/4:1	79/1:1
5	**5**	**12**	80/1:1	82/1:1
6	**6**	**13**	81/≈1:19	88/1:4

[a] α/β ratios were determined from the integral ratios of the reducing-end anomeric proton signals (ca. 5.5 ppm); ≈1:19 α/β ratios have been given for samples in which no signals arising from α-anomers were observed. [b] Glycosylations were performed in CH_2Cl_2/CH_3CN/EtCN solvent mixtures (1:2:1) at 10–15 mM substrate concentrations. [c] Glycosylations were performed in CH_2Cl_2 solvent at 50 mM substrate concentrations.

tains the *trans*-directing property. The 2-deoxy thioglucoside **5** was accordingly prepared and used for glycosylation of **7** both in the 1:1:1 CH_2Cl_2/CH_3CN/EtCN solvent mixture and in CH_2Cl_2. However, no glycosylation selectivity was detected in either case (Table 1, entry 5). Interestingly, whenever a C-2 ether function is present, the *trans*-directing property is apparent, as illustrated in the glycosylation of **7** with the L-thiofucosyl donor **6** (Table 1, entry 6).

Preliminary evidence for the formation of glycosyl oxazolinium intermediates: The key element in the proposed C-2 ether participation is the formation of glycosyl oxazolinium intermediates, so it is crucial to provide evidence for their existence. In anticipation of their poor stability, direct isolation of such an intermediate seems impractical. As an alternative, a simulated glycosylation experiment was designed to trap a derivative of such an intermediate. For this purpose, we used a thioglycosyl donor with a free C-2 hydroxy group. Our rationale is that if such a donor was activated under LCG conditions, the C-2 OH function of the donor should react with the *cis*-oriented nitrile molecule to form an oxazolinium intermediate. This intermediate could however be transformed into a less reactive oxazoline for isolation. Thus, the isolation of the oxazoline, as a debenzylation product of the oxazolinium species, would provide indirect evidence for the existence of the oxazolinium species.[28]

The thioglycosyl donors **14**, **15**, and **16** (Scheme 1) were thus synthesized by standard methods and subjected to the simulated glycosylation experiment in CH_2Cl_2/EtCN mixtures, in which no acceptor was added.[29] To our delight, the reactions furnished the expected glycosyl oxazolines **17**, **18**, and **19** in yields ranging from 15% to 70%.[30] The chemical identities of **17**, **18**, and **19** were supported by 1) characteristic proton/carbon NMR signals, and 2) HRMS.[28] Because



Scheme 1. Preparation of the glycosyl oxazolines **17–19** from the unprotected C-2 hydroxy thioglycoside donors **14–16**.

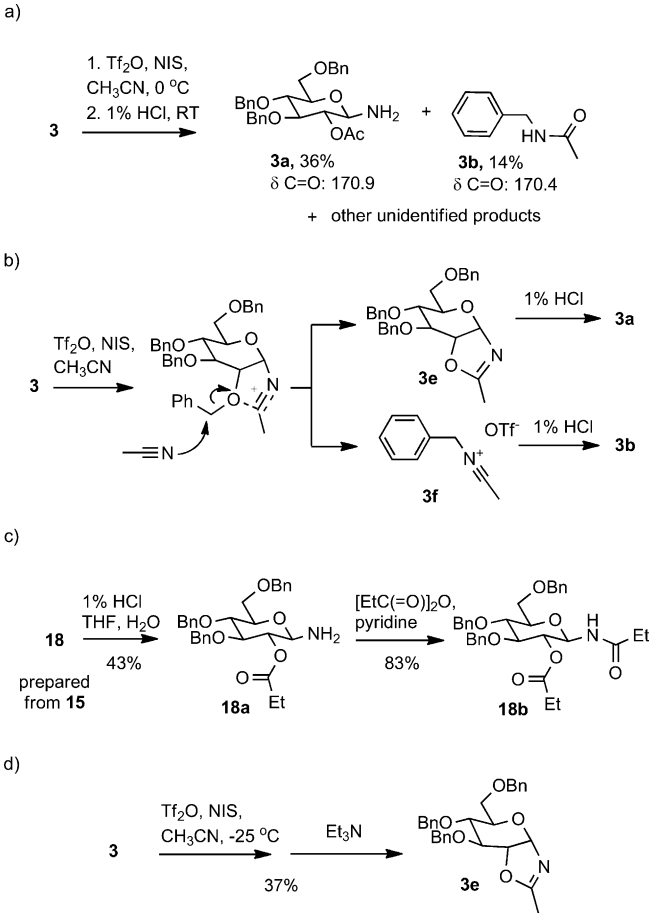
we have demonstrated the formation of the oxazolines from their thioglycoside precursors, the proposed oxazolinium intermediates in glycosylations is justified. However, it should be pointed out that the C-2 unprotected donors described above are different from fully protected glycosyl donors and therefore, it would be premature to extrapolate a conclusive statement from present experimental data. Nevertheless, the above data do support a conceptual possibility, which motivated further investigations for searching additional evidence.

Formation of glycosyl oxazolinium intermediates from fully protected thioglycosides: In 1981, Pavia reported the synthesis of glucosylamine from glucosyl hemiacetal in acetonitrile. The reaction was presumed to proceed through an oxazolinium formation step, although no mechanistic studies were performed to confirm the hypothesis.[31] We speculated that by adoption of their experimental protocol it might be possible to obtain the putative oxazolinium intermediate from a fully protected thioglucoside.

To put this idea into practice, the perbenzyl thioglucoside **3** (Table 1) was activated in acetonitrile by treatment with triflic anhydride (Tf_2O) and NIS in the absence of the acceptor. Upon activation of the thioglycoside, the reaction was quenched by addition of aq. HCl (1%). After workup and chromatographic purification, the 2-*O*-acetyl glucosylamine **3a** (Scheme 2a, ca. 36%) was obtained, together with *N*-benzylacetamide (**3b**, ca. 14%). Because of their close molecular polarities the separation of **3a** and **3b** was nontrivial. The yield of **3b** was lower than that of **3a**, which might be attributable to attack on the oxazolinium species by other adventitious nucleophiles in the system (Scheme 2a). The chemical identities of **3a** and **3b** were verified by NMR spectroscopy and mass spectrometry. It is worth noting that the β-anomeric configuration of **3a** is attributable to a known sterically driven (α→β) isomerization of the free amino function.[32]

At this stage, we outlined a mechanism for the formation of **3a** and **3b** (Scheme 2b) with reference to Pavia's proposal. Activation of **3** in the nitrile solvent could produce an oxazolinium intermediate through C-2 ether participation. Such an intermediate could be attacked by acetonitrile to produce the oxazoline intermediate **3e** and the benzyl nitrilium species **3f**. Subsequent acid hydrolysis of **3e** and **3f** would furnish the isolated products **3a** and **3b**. To corroborate this interpretation, we first prepared the glucosyl oxazoline **18** (Scheme 1) from the thioglucoside **15** in EtCN by our developed protocol. Compound **18** was then treated with aq. HCl (1%) as in Scheme 2c. To our delight, the expected 2-*O*-propionyl-β-glucosylamine **18a** was generated in 43% yield. For reasons of stability **18a** was converted into the 2-*O*-propionyl-β-*N*-glucosyl propionamide **18b**.

After proving the formation of the glycosylamine from the glycosyl oxazoline, we next moved on to procure the glucosyl oxazoline from a fully protected thioglycoside (Scheme 2d). Such a result would confirm the existence of an oxazolinium intermediate, because the oxazoline is a



Scheme 2. a) Formation of the 2-*O*-acetyl glucosylamine **3a** and *N*-benzylacetamide (**3b**). b) Mechanism for the formation of **3a** and **3b**. c) Acid hydrolysis of the glucosyl oxazoline **18**. d) Synthesis of the glucosyl oxazoline **3e** from fully protected **3**.

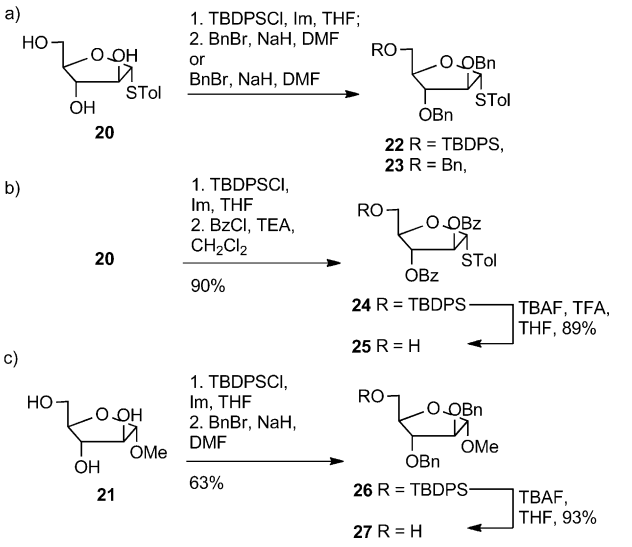
dealkylation product of the oxazolinium species. Tf_2O/NIS activation of **3** was thus repeated at a lower temperature (−25 °C). Upon completion of activation, triethylamine was added to quench the reaction in place of the HCl solution (Scheme 2d). After workup, the desired oxazoline **3e** was obtained in a satisfactory 37% yield.[33] Taken together, the results shown in Scheme 2a,c, and 2d clearly support the presence of oxazolinium intermediates in glycosylations involving participation by nitrile solvents.

At this point, one might ask why the "dealkylation at the C-2 position" does not occur when a hydroxy acceptor is present under standard LCG conditions. One possible explanation is that when a hydroxy acceptor is present, it preferentially attacks at the anomeric carbon to form a stable product. In hindsight, these findings explain the failure of an earlier attempt to apply the LCG conditions to a preactivation glycosylation protocol. A similar failure in glycosylations had previously been reported by Crich when a preactivation protocol was conducted in 100% EtCN.[15]

Application to α(1→5)-arabinan synthesis: After having established the participating role of the C-2 ether-protecting function, we next applied this property for 1,2-*trans* glycosidic bond formation. As the synthetic targets we chose α(1→5)-arabinan oligomers. These oligomers constitute a major class of cell wall components in *Mycobacterium tuberculosis*.[34–37] Because of their biological relevance and the demand for pure arabinans for synthesis of more complex oligosaccharides, an efficient preparation method is desirable and necessary. Previous syntheses of α(1→5)-arabinan have often employed C-2 ester-protected arabinosyl donors for construction of the α-glycosidic linkage.[38–42] It was speculated that this linkage might be accessible from an arabinosyl donor bearing a C-2 ether-protecting function when the coupling reaction is conducted in a nitrile solvent. An advantage of using a C-2 ether-protected arabinosyl donor is that such a donor is more reactive than a C-2 ester-protected one.[43,44] This reactivity disparity provides access to a reactivity-based one-pot synthesis of α-(1→5)-arabinans.[44]

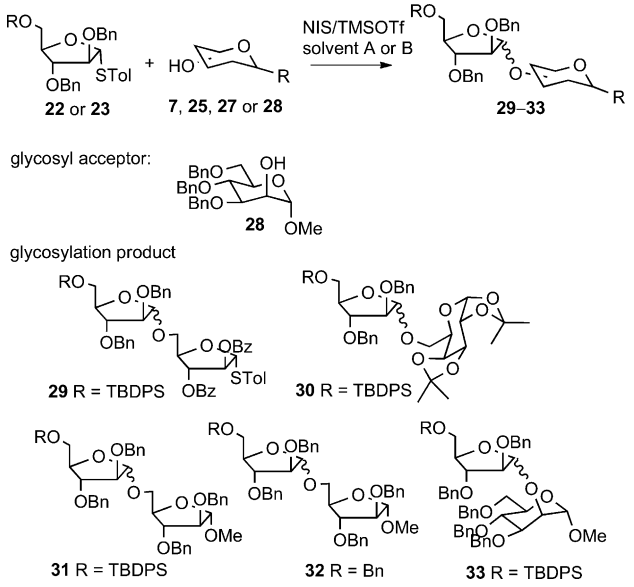
Before initiating the synthesis of arabinan, we first assessed the alpha-selectivity of C-2 ether-protected arabinosyl donors in glycosylations under LCG conditions. To this end, series of arabinosyl building blocks **22–27** were required and they were prepared from known arabinosides, **20** and **21**, by literature methods (Scheme 3a–c).[38-42] Noted in removal of the C-5 silyl ether function in the thioarabinoside 24, a stoichiometric amount of trifluoroacetic acid (TFA) was added to prevent the migration of benzoyl ester functions (Scheme 3b).[39]

After preparing the arabinosyl building blocks, the stage was ready for assessing the glycosylation selectivity. Initially, different reaction conditions for glycosylation of the thioarabinoside **25** with the thioarabinoside **22** were examined (Table 2, entries 1–5). The 1,2-*trans*-directing effect of the C-2 ether function was apparent when a 1:2:1 CH_2Cl_2/CH_3CN/EtCN solvent mixture was used (Table 2, entries 1–2). As expected, the highest selectivity of glycosylation was achieved under the LCG conditions, and the desired disaccharide **29** was furnished in an α/β-anomeric ratio of 10:1



Scheme 3. Preparation of the arabinosyl building blocks **22**, **23**, **25**, and **27**.

Table 2. Glycosylations of the glycosyl acceptors **7**, **25**, **27**, and **28** with the thioarabinofuranosyl donors **22** and **23**.



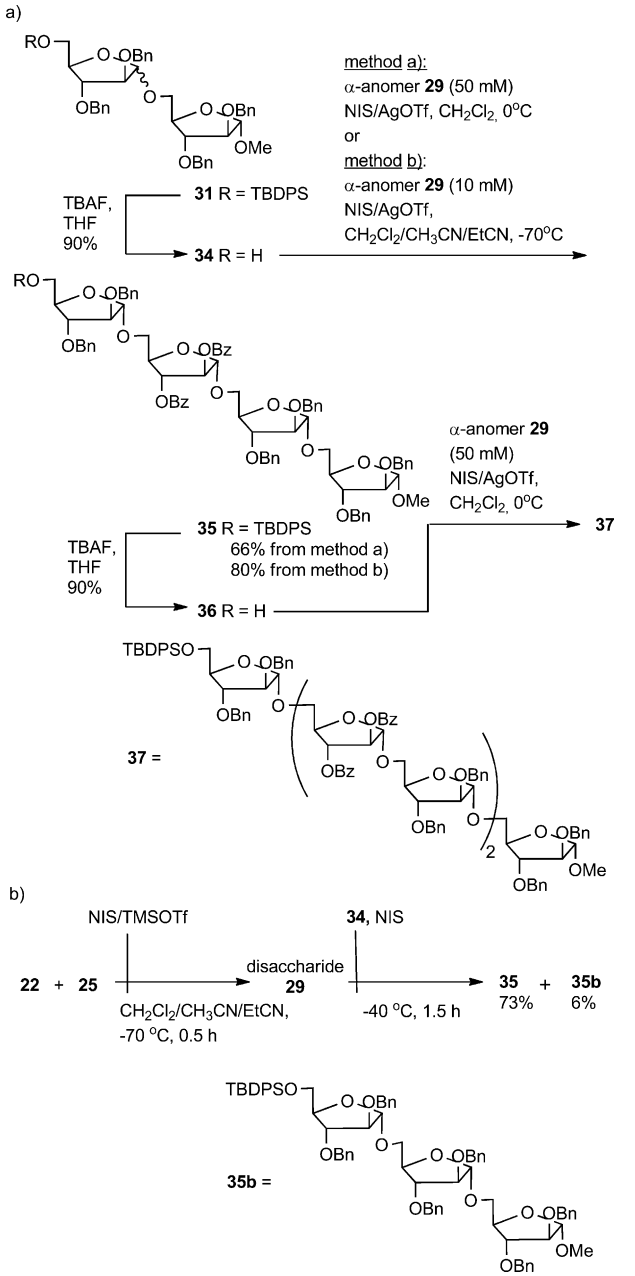
	Donor	Acceptor (c [mM])	T [°C]	Solvent[a]	Product/Yield [%]/ α:β[b]
1	**22**	**25** (20)	−55	A	**29**/85/3/2
2	**22**	**25** (20)	−55	B	**29**/89/7:1
3	**22**	**25** (20)	−10	B	**29**/75/5:1
4	**22**	**25** (50)	−70	B	**29**/70/5:1
5	**22**	**25** (10)	−70	B	**29**/85/10:1
6	**22**	**7** (10)	−70	B	**30**/80/10:1
7	**22**	**27** (50)	−70	A	**31**/95/2:1
8	**22**	**27** (10)	−70	B	**31**/96/12:1
9	**23**	**27** (50)	−70	A	**32**/95/1:1.5
10	**23**	**27** (10)	−70	B	**32**/80/9:1
11	**22**	**28** (10)	−70	B	**33**/68/3:1

[a] Solvent A was CH_2Cl_2; solvent B was CH_2Cl_2/CH_3CN/EtCN 1:2:1. [b] α/β-anomer ratio was determined by ^1H NMR spectroscopy.

(Table 2, entries 2–5). The configuration of the α-glycosidic bond in **29** was confirmed by the chemical shifts of the anomeric proton at 5.16 ppm and the anomeric carbon at 106.2 ppm, which fully agrees with with the literature values.[38] High α-selectivity of glycosylation was observed for the glycosyl acceptors **7** and **27** (Table 2, entries 6–8). In addition, the method is also effective for other thioarabinosyl donors, such as **23**, which bears a smaller benzyl protecting function at the C-6 position (Table 2, entries 9, 10). Although the glycosylation of the secondary mannosyl acceptor **28** afforded only modest α-selectivity (Table 2, entry 11),[46] It may be attributable to a mismatching coupling between the glycosyl donor and acceptor.[47–49]

After confirming the efficiency of the 1,2-*trans*-directing effect of the C-2 ether function, the synthesis of the target arabinans was carried out. For the purpose of comparison, both convergent and one-pot glycosylation strategies were examined. Although Liang et al. has recently reported on one-pot orthogonal glycosylation for the synthesis of α-(1→5)-arabinans, no reactivity-based one-pot glycosylation strategy has yet been developed.[41] The advantage of this strategy is to eliminate the need for orthogonal anomeric functions.[44,45] We thus made use of the reactivity difference between the more reactive thioarabinoside **25** to effect a reactivity-based one-pot synthesis of α-(1→5)-arabinan.[43]

In a [2+2] convergent approach, the reducing-end disaccharide **34** (Scheme 4a) was prepared by removal of the silyl ether protecting group in the disaccharide arabinofuranoside **31**. Subsequent glycosylation of **34** with the α-anomer of the thioarabinoside **29** was performed under conventional conditions and LCG conditions. The yield of the desired arabinan tetramer **35** obtained through conventional conditions was significantly lower than through LCG conditions (66%



Scheme 4. a) Convergent syntheses of the arabinan tetramer **35** and the hexamer **37**. b) Reactivity-based one-pot synthesis of the arabinan tetramer **35**.

by conventional conditions versus 80% by LCG; Scheme 4a). The chemical shifts of the anomeric carbons of **35** were identified at 5.31 (for H-1″), 5.17 (for H-1‴), 5.16 (for H-1′), and 4.91 ppm (for H-1), which agree with literature values.[38,41] Further optimization of the reaction temperature (to −40 °C) improved the yield of **35** to 83%. Apparently, the LCG conditions avoid some side-reactions resulting from the highly reactive oxocarbenium ion.

Similarly, the synthesis of a larger arabinan oligomer could simply be achieved by: 1) removing the silyl ether function at C-5 in the arabinan tetramer **35** to form a tetrasaccharide acceptor **36**; and 2) glycosylation coupling of the acceptor **36** with the disaccharide thioarabinoside **29** to yield desired arabinan hexamer **37** (Scheme 4a).

With the optimized reaction conditions now established, we attempted the reactivity-based one-pot synthesis of arabinan tetramer. The reactive thioarabinoside **22** was first treated with the less reactive thioarabinoside **25** under LCG conditions (Scheme 4b). The glycosylation coupling went smoothly to furnish the disaccharide thioarabinoside **29**. Without isolation, the thioarabinoside **29** was directly coupled with the reducing-end disaccharide **34** under the promotion of NIS/TMSOTf to yield the desired arabinan tetramer **35** in an excellent 73% yield (over two glycosylation steps). A concern in this one-pot reaction would be contamination with the undesired β-anomer, which might be produced during the first glycosylation step. To our delight, though, the tetramer **35**, obtained by the one-pot glycosylation was of high purity with no detectable trace of the undesired anomer (NMR scale). For illustration, the enlarged ^{13}C NMR spectrum at the anomeric region of the tetramer **35** is shown in Figure 2. It should be pointed out, that a small amount (6%) of the arabinan trimer **35b**, the product of a coupling reaction between excess thioarabinoside **22** and the disaccharide **34**, was obtained.

Conclusion

This article reports the participation of a C-2 ether function in glycosylation reactions, when these reactions are conducted under LCG conditions. Further experimental data suggest the formation of glycosyl oxazolinium intermediates through the participation of the ether function. Accordingly, a revised mechanism for glycosylations in nitrile solvents is proposed for the first time. Application of this participation concept has enabled an efficient convergent and one-pot synthesis of biologically relevant α-(1→5)-arabinan oligomers.

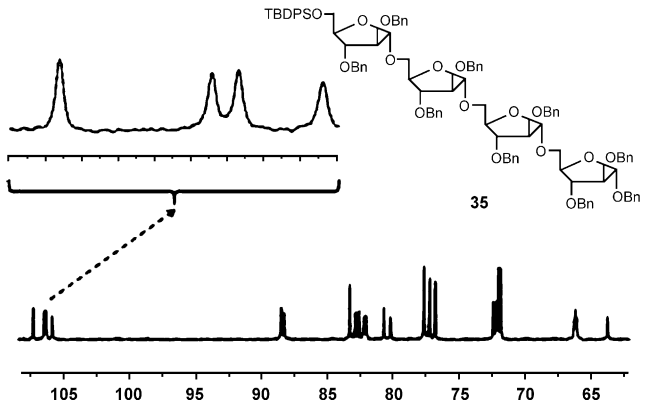


Figure 2. Expanded ^{13}C NMR spectrum of **35** in the anomeric region.

Experimental Section

General: All solvents for reactions were purchased as ACS grade from commercial vendors. Glycosylation solvents CH_2Cl_2 and CH_3CN were dried with a solvent purification system (AWS-1000). Dry propionitrile was obtained by distillation over calcium hydride. Reagents for chemical reactions were used directly without further purifications. Chemical reactions were monitored by thin layer chromatography (TLC) on silica gel plates (E. Merck, 0.25 mm, 60F-254). Compounds on TLC plates were visualized by UV absorption and/or by staining with ceric ammonium molybdate or acidic *p*-anisaldehyde solution. Flash column chromatography was performed on silica gel (E. Merck, Si-60, particle size 0.063 to 0.200 mm). NMR spectra were recorded with Bruker DRX 300, Varian Unity 300 (300 MHz for ^1H, 75 MHz for ^{13}C), or Varian UI 500 (500 MHz for ^1H, 125 MHz for ^{13}C) instruments. Crude product mixtures in EtOAc (10 μL, 2–5 wt%) were loaded onto Mightysil Si 60 250–4.6 columns. EtOAc/hexane solvent mixtures was used as eluents for sample elution at 0.8 mL min^{-1} flow rate. The galactosyl acceptor **7** is commercially available. The preparations of the glycopyranosides **1**–**6**, **14**–**16**, and **28** and of the arabinofuranosides **22**–**27** are detailed in the Supporting Information.

General LCG procedure for the disaccharides 8–13:[10] A mixture of the thioglycoside **1**, **2**, **3**, **4**, **5**, or **6** (0.23 mmol, 1.2 equiv), the galactosyl acceptor **7** (0.19 mmol, 1.0 equiv), and molecule sieves (flame-dried, AW300) in CH_2Cl_2/CH_3CN/EtCN (1:2:1) was cooled to −70 °C and stirred under N_2 for ca. 30 min (exact amounts of reagents and specific reaction conditions are detailed in Table S1 in the Supporting Information). NIS (0.24 mmol, 1.25 equiv) and TMSOTf (0.05 mmol, 0.24 equiv) were added sequentially to the reaction mixture. After completion of the reaction (TLC), the reaction mixture was treated with a few drops of Et_3N and satd. aq. $NaHCO_3$ and with $Na_2S_2O_3$ (s). The reaction mixture was then stirred vigorously until the color of the solution had changed from deep red to pale yellow, and the crude reaction product was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The desired disaccharides **8**–**13** were obtained after column chromatographic purification.

Synthesis of 2,3,4,6-tetra-*O*-benzyl-β-D-galactopyanosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (8): The disaccharide **8** was obtained after chromatographic purification (elution: hexane/EtOAc/CH_2Cl_2 6:1:0 to 1.5:1:1) as a white amorphous solid (120 mg, α/β ≈1:19, 80%). R_f=0.2 (hexane/EtOAc 4:1); ^1H NMR (300 MHz, $CDCl_3$): δ= 7.54 (d, *J*=6 Hz, 2H; ArH), 7.45–7.35 (m, 18H; ArH), 5.65 (d, *J*=3 Hz, 1H; H-1), 5.15 (d, *J*=10.8 Hz, 1H), 5.08 (d, *J*=11.7 Hz, 1H), 4.89–4.76 (q, *J*=12.4 Hz, 4H), 4.71–4.64 (m, 2H), 4.4–4.45 (m, 3H), 4.39–4.37 (dd, *J*=2, 4.5 Hz, 1H), 4.30 (d, *J*=7.8 Hz, 1H), 4.25–4.13 (m, 2H), 3.97–3.89 (m, 2H), 3.82–3.76 (m, 1H), 3.68–3.57 (m, 4H), 1.60 (s, 3H; CH_3), 1.52 (s, 3H; CH_3), 1.38 ppm (s, 6H; $CH_3\times2$); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 139.5, 139.1, 138.4, 129.1, 128.89, 128.88, 128.8, 128.7, 128.6, 128.4, 128.3, 127.98, 127.91, 127.9, 127.8, 109.7 ($C(CH_3)_2$), 109.1 ($C(CH_3)_2$), 105.1 (C-1′), 96.4 (C-1), 82.3, 79.5, 75.2, 74.9, 73.9, 73.7, 73.5, 71.9,71.2, 70.9, 70.1, 69.1, 67.8, 26.5 (CH_3), 26.4 (CH_3), 25.5 (CH_3), 24.9 ppm (CH_3).[10]

Synthesis of 2,3,4,6-tetra-*O*-methyl-β-D-galactopyanosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (9): The disaccharide **9** was obtained after chromatographic purification (elution: hexane/EtOAc/CH_2Cl_2 8:1:1 to 3:1:1) as a white amorphous solid (70 mg, α/β ≈1:19, 77%). R_f=0.15 (hexane/EtOAc 2:1); ^1H NMR (300 MHz, $CDCl_3$): δ=

5.51 (d, $J=6$ Hz, 1H; H-1), 4.57 (dd, $J=2.4$ Hz, $J=7.8$ Hz, 1H), 4.31–4.26 (m, 2H), 4.20 (dd, $J=1.8$, 7.8 Hz, 1H), 4.10–3.98 (m, 2H), 3.65–3.47 (m, 14H; $OCH_3\times3$), 3.37 (s, 3H; OCH_3), 3.34–3.28 (m, 1H), 3.14 (dd, $J=3$, 10 Hz, 1H), 1.47 (s, 3H; CH_3), 1.42 (s, 3H; CH_3), 1.30 ppm (s, 6H; $CH_3\times2$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=109.1$ ($C(CH_3)_2$), 108.5 ($C(CH_3)_2$), 104.0 (C-1′), 96.1 (C-1), 83.1, 80.4, 74.6, 72.6, 71.2, 70.5, 70.3, 68.9, 67.5, 61.1, 60.6, 59.07, 58.18, 29.4 (CH_3), 25.8 (CH_3), 24.9 (CH_3), 24.2 ppm (CH_3); HRMS: m/z calcd for $C_{22}H_{40}O_9Na$ $[M+Na]^+$: 501.2306; found: 501.2332. Compound **9** was contaminated with inseparable succinimide (^{1}H NMR: $\delta=9.14$ (br s, NH), 2.74 ppm (s, $CH_2\times2$); ^{13}C NMR: $\delta=178$ (C=O), 29.5 ppm ($CH_2\times2$)).

Synthesis of 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyanosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (10):[50] The disaccharide **10** was obtained as a white amorphous solid (123 mg, α/β ≈1:19, 83%) after chromatographic purification (elution: hexane/EtOAc/CH_2Cl_2 8:1:1 to 3:1:1). ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.44$–7.41 (m, 2H; ArH), 7.30–7.22 (m, 18H; ArH), 7.14–7.12 (m, 2H; ArH), 5.57 (d, $J=6$ Hz, 1H), 5.05 (d, $J=11.1$ Hz, 1H), 4.96 (d, $J=10.8$ Hz, 1H), 4.82–4.70 (m, 3H), 4.64–4.45 (m, 5H), 4.33–4.30 (m, 1H), 4.24 (dd, $J=1.8$, 7.8 Hz, 1H), 4.16 (dd, $J=2.4$, 10.5 Hz, 1H), 4.11–4.08 (m, 1H), 3.76–3.38 (m, 5H), 3.49–3.44 (m, 2H), 1.50 (s, 3H; CH_3), 1.42 (s, 3H; CH_3), 1.30 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=138.6$, 138.1, 128.6, 128.3, 128.1, 127.9, 127.8, 127.7, 127.54, 127.47, 127.42, 109.3 ($C(CH_3)_2$), 108.5 ($C(CH_3)_2$), 104.3 ($J_{C,H}=160$ Hz, C-1′), 96.3 ($J_{C,H}=172$ Hz, C-1), 84.5, 81.6, 77.7, 75.6, 74.9, 73.4, 71.4, 70.4, 69.6, 68.7, 67.3, 26.0, 25.95, 24.97, 24.4 ppm.

Synthesis of 2,3,4,6-tetra-*O*-benzyl-D-mannopyanosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (11):[51] The disaccharide **11** was obtained after chromatographic purification (elution: hexane/EtOAc/CH_2Cl_2 8:1:2 to 2:1:1) as a colorless syrup (112 mg, inseparable 3:1 α/β-anomeric mixture, 82%). The α/β ratio was calculated from the integral areas of the reducing-end proton at 5.67 and 5.59 ppm. ^{1}H and ^{13}C NMR spectra of the α/β-anomeric mixture of **11** are given in the Supporting Information for reference.

Synthesis of 3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyanosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (12):[52] The disaccharide **12** was obtained after chromatographic purification (elution: hexane/EtOAc/CH_2Cl_2 8:1:2 to 2:1:1) as a colorless syrup (104 mg, 80%, inseparable 1:1 α/β-anomeric mixture). The α/β ratio was calculated from the integral areas of the reducing-end proton at 5.60 and 5.56 ppm. ^{1}H and ^{13}C NMR spectra of the α/β-anomeric mixture of **12** are given in the Supporting Information for reference.

Synthesis of 2,3,4-tri-*O*-benzyl-β-L-fucopyanosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (13):[52] The disaccharide **13** was obtained after chromatographic purification (elution: hexane/EtOAc/CH_2Cl_2 8:1:2 to 2:1:1) as a colorless syrup (103 mg, 81%). For the β-anomer of **13**: $R_f=0.3$ (hexane/EtOAc 4:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.45$–7.28 (m, 15H; Ar), 5.54 (d, $J=6$ Hz, 1H; H-1), 5.02 (d, $J=11.4$ Hz, 2H), 4.84–4.71 (m, 4H), 4.60 (dd, $J=2.4$, 8.1 Hz, 1H), 4.40 (d, $J=7.8$ Hz, 2H), 4.37 (dd, $J=2.4$, 5.1 Hz, 1H), 4.12–4.01 (m, 2H), 3.88–3.79 (m, 2H), 3.58–3.46 (m, 3H), 1.55 (s, 3H; CH_3), 1.47 (s, 3H; CH_3), 1.35 (s, 3H; CH_3), 1.31 (s, 3H; CH_3), 1.19 ppm (d, $J=6.3$ Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=138.8$, 138.5, 138.4, 128.6, 128.3, 128.2, 128.21, 128,15, 128.1, 127.8, 127.53, 127.51, 127.4, 108.9 ($C(CH_3)_2$), 108.5 ($C(CH_3)_2$), 104.1 (C-1′), 96.2 (C-1), 82.3, 79.3, 76.0, 74.9, 74.5, 73.1, 70.7, 70.5, 70.4, 70.3, 67.5, 65.9, 26.03 (CH_3), 25.9 (CH_3), 24.9 (CH_3), 24.4 (CH_3), 16.8 ppm (CH_3).

General procedure for formation of the glycosyl oxazolines 17–19: A mixture of the C-2-unprotected thioglycoside **14**, **15**, or **16** (0.27 mmol, 1.0 equiv) and molecule sieves (flame-dried, AW300) in a 1:3 CH_2Cl_2/EtCN solvent mixture (24 mL) was cooled to −70 °C and stirred at that temperature for about 20 min to 1 hour under N_2 (exact amounts of reagents and specific reaction conditions are detailed in Table S2 in the Supporting Information). NIS (0.29 mmol, 1.1 mol equiv) and TMSOTf (0.053 mmol, 0.2 mol equiv) were added to the reaction mixture. The reaction temperature was then slowly adjusted to a suitable level to accelerate the oxazoline formation. One hour after the disappearance of the starting material (TLC), the reaction mixture was treated with NEt_3 (ca. 0.3 mL), followed by addition of few drops satd. aq. $NaHCO_3$ (5%, v/v of reaction volume) and a small piece of $Na_2S_2O_3$ (s). The resulting mixture was stirred at RT until the color of solution had changed from garnet to pale yellow. The resulting solution was then dried (over $MgSO_4$), filtered, and concentrated for column chromatographic purification over preneutralized SiO_2 (neutralization of SiO_2: elution with eluting solvent plus 5% Et_3N) to furnish the desired glycosyl oxazolines **17** and **19**. A modified workup protocol was adopted for oxazoline **18**: after disappearance of **15** (judged by TLC), the reaction mixture was treated with Et_3N, a few drops of saturated $NaHCO_3$, and small pieces of solid $Na_2S_2O_3$. The resulting mixture was irradiated with ultrasonic waves at RT for few minutes (Model: Delta 2198, DC 300) until the color of the mixture changed to pale yellow. Subsequent steps were similar to those for oxazolines **17** and **19**, the desired oxazoline **18** was obtained after purification by chromatography.

Synthesis of (3a*S*,5*R*,6*S*,7*S*,7a*R*)-6,7-bis(benzyloxy)-5-[benzyloxymethyl]-2-ethyl-5*H*-pyrano[2,3-*d*]oxazole (17): The oxazoline **17** was prepared from the C-2 unprotected thioglycoside **14** and obtained after chromatographic purification (elution: hexane/EtOAc/CH_2Cl_2 3:1:1 to 1.5:1:1) as a colorless syrup (60 mg, 45%). $R_f=0.25$ (hexane/EtOAc 1:1); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.40$–7.28 (m, 15H; Ar), 5.77 (d, $J=6$ Hz, 1H; H-1), 4.96 (d, $J=11.4$ Hz, 2H), 4.77 (d, $J=12.3$ Hz, 1H), 4.73–4.62 (m, 3H), 4.54–4.41 (m, 2H), 4.11–4.10 (m, 1H), 4.04–3.99 (m, 1H), 3.76–3.70 (m, 1H), 3.67–3.62 (m, 2H), 2.36 (q, $J=7.5$ Hz, 2H; CH_2), 1.21 ppm (t, $J=7.5$ Hz, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=173.1$ 138.3, 137.9, 128.4, 128.3, 128.2, 127.8, 127.76, 127.72, 127.67, 127.62, 127.53, 93.0 (C-1), 81.8, 79.4, 74.5, 73.5, 73.4, 72.9, 71.2, 67.8, 21.9 (CH_2), 9.9 ppm (CH_3); HRMS: m/z calcd for $C_{30}H_{34}NO_5$ $[M+H]^+$: 488.2432; found: 488.2436.

Synthesis of (3a*S*,5*R*,6*R*,7*S*,7a*R*)-6,7-bis(benzyloxy)-5-[benzyloxymethyl]-2-ethyl-5*H*-pyrano[2,3-*d*]oxazole (18): The oxazoline **18** was prepared from the C-2-unprotected thioglycoside **15** and was obtained after chromatographic purification (elution: hexane/EtOAc/CH_2Cl_2 3:1:1 gradient to 1:1:1) as a colorless oil (92 mg, 70%). $R_f=0.2$ (hexane/EtOAc 1:1, plus 5% Et_3N); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.38$–7.29 (m, 13H; Ar), 7.22–7.19 (m, 2H; Ar), 5.89 (d, $J=7.5$ Hz, 1H; H-1), 4.78 (d, $J=12$ Hz, 1H), 4.69–4.65 (m, 2H), 4.62–4.58 (m, 1H), 4.50–4.45 (m, 3H), 3.79–3.74 (m, 2H), 3.70 (d, $J=3$ Hz, 1H), 3.58–3.55 (m, 1H), 2.35 (q, $J=7.5$ Hz, 2H; CH_2), 1.20 ppm (t, $J=7.5$ Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=172.0$, 137.9, 137.7, 128.3, 128.2, 127.87, 127.86, 127.75, 127.7, 127.5, 93.4 (C-1), 80.3, 79.5, 74.3, 73.5, 73.3, 72.2, 71.3, 69.3, 21.7 (CH_2), 9.9 ppm (CH_3); HRMS: m/z calcd for $C_{30}H_{34}NO_5$ $[M+H]^+$: 488.24315; found: 488.24363.

Synthesis of (3a*R*,5*R*,6*R*,7*S*,7a*R*)-6,7-bis(benzyloxy)-5-[benzyloxymethyl]-2-ethyl-5*H*-pyrano[2,3-*d*]oxazole (19): The oxazoline **19** was prepared from the C-2 unprotected thioglycoside **16** and obtained after chromatographic purification (elution: hexane/EtOAc/CH_2Cl_2 3:1:1 to 1:2:1) as a colorless syrup (22 mg, 15%). $R_f=0.15$ (hexane/EtOAc 1:2); crude ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.31$–7.27 (m, 15H; Ar), 5.45 (d, $J=3.9$ Hz, 1H; H-1), 4.77–4.60 (m, 2H), 4.56–4.48 (m, 4H), 3.94–3.89 (m, 2H), 3.66–3.63 (m, 4H), 2.40 (q, $J=7.8$ Hz, 2H; CH_2), 1.22 ppm (t, $J=7.8$ Hz, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=174.4$, 138.2, 137.9, 137.8, 128.45, 128.36, 128.32, 128.27, 128.2, 128.03, 128.01, 127.95, 127.93, 127.84, 127.77, 127.7, 127.6, 127.5, 127.42, 127.39, 127.36, 127.3, 127.2, 93.0 (C-1), 78.4, 77.2, 76.4, 76.0, 75.0, 74.0, 73.4, 72.8, 70.3, 21.7 (CH_2), 9.9 ppm (CH_3); HRMS: m/z calcd for $C_{30}H_{34}NO_5$ $[M+H]^+$: 488.24315; found: 488.24521. NMR spectra of **19** were contaminated with succinimide (a known byproduct of NIS), and further purification of **19** was precluded for reasons of stability.

Synthesis of 2-*O*-acetyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranosylamine (3a):[28,31] Tf_2O (77 μL, 0.46 mmol) was added at 0 °C under N_2 to a cooled solution of the thioglucoside **3** (300 mg, 0.46 mmol) in CH_3CN (9 mL). After the mixture had been stirred for 1 hour, NIS (110 mg, 0.49 mmol) was added. Upon completion of the activation of **3**, aq. HCl (1%, 1 mL) was added. The crude mixture was then extracted with EtOAc (15 mL) and NaOH (1 N, 15 mL). The combined organic layer was then treated with sat. $NaHCO_3$ (0.3 mL) and $Na_2S_2O_3$ (s, ca. 1.5 g). The crude reaction product was stirred vigorously at RT. After the crimson color of the mixture had turned to pale yellow, the mixture was then

separated, dried (over $MgSO_4$), filtered, and concentrated for chromatography purification (elution: EtOAc/hexane/CH_2Cl_2 1:2:1 to 3:1:1) to furnish the glucosylamine **3a** as a yellow foam (55 mg, 36%). R_f=0.33 (EtOAc/CH_2Cl_2 1:8); ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.35–7.26 (m, 13H; Ar), 7.14–7.11 (m, 2H; Ar), 4.85–4.47 (m, 7H), 4.08 (d, J=9 Hz, 1H; H-1), 3.73–3.63 (m, 4H), 3.54–3.50 (m, 1H; H-5), 1.99 (s, 3H; CH_3), 1.94 ppm (br, NH_2); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=170.9, 138.7, 138.3, 138.26, 129.1, 128.9, 128.43, 128.37, 128.28, 128.18, 128.14, 128.10, 127.97, 85.3(C-1), 84.1, 78.6, 76.2, 75.6, 75.4, 74.8, 73.9, 65.3 (C-6), 21.5 ppm (C-(CH_3)$_3$).

Synthesis of (3a*S*,5*R*,6*R*,7*S*,7a*R*)-6,7-bis(benzyloxy)-5-[benzyloxymethyl]-2-methyl-5*H*-pyrano[2,3-*d*]oxazoline (3e) from the fully protected thioglucoside 3:[28] Tf_2O (77 μL, 0.46 mmol) was added at −25°C under N_2 to a cooled solution of the thioglucoside **3** (300 mg, 0.46 mmol) in CH_3CN (16 mL). After the mixture had been stirred for 1 h, NIS (110 mg, 0.49 mmol) was added. Upon completion of activation of **3**, triethylamine (0.5 mL) was added. The crude mixture was then treated with sat. $NaHCO_3$ (0.3 mL) and $Na_2S_2O_3$ (s, ca. 1.5 g) and stirred vigorously at RT. After the crimson color of the mixture had turned to pale yellow, the mixture was then separated, dried (over $MgSO_4$), filtered, and concentrated for standard chromatography purification (elution: EtOAc/hexane/CH_2Cl_2 1:3:1 to 2:1:1, the silica gel was pre-neutralized as described before) to furnish the glucosyl oxazoline **18a** as a colorless syrup (79 mg, 37%).

Synthesis of *p*-tolyl 2,3-di-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)thio-α-D-arabinofuranoside (22):[42] The preparation procedure is given in the Supporting Information. R_f=0.3 (EtOAc/hexane 1:15); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.68–7.64 (m, 4H; Ar), 7.42–7.25 (m, 18H; Ar), 7.10–7.07 (m, 2H; Ar), 5.51 (d, J=2.4 Hz, 1H; H-1), 4.60 (d, J=11 Hz, 1H), 4.54–4.49 (m, 3H), 4.31 (m, 1H), 4.12 (d, J=3 Hz, 2H), 3.89–3.78 (m, 2H), 2.32 (s, 3H; CH_3), 1.04 ppm (s, 9H; *t*Bu); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=137.7, 137.4, 137.1, 135.61, 135.55, 133.2, 133.3, 131.8, 131.1, 129.6, 128.33, 128.29, 127.8, 127.7, 127.6, 127.5, 90.4 (C-1), 88.3, 83.1, 81.9, 72.1, 63.3, 72.0, 26.7 (C(CH_3)$_3$), 21.1, 19.2 ppm (C(CH_3)$_3$).

Synthesis of *p*-tolyl 2,3,5-tri-*O*-benzylthio-α-D-arabinofuranoside (23):[53] The procedure is given in the Supporting Information. R_f=0.3 (EtOAc/hexane 1:15); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.42–7.39 (m, 2H; Ar), 7.32–7.27 (m, 15H; Ar), 7.11–7.08 (m, 2H; Ar), 5.55–5.54 (m, 1H), 4.65–4.46 (m, 6H), 4.41–4.37 (m, 1H), 4.12–4.10 (m, 1H), 4.05–4.02 (m, 1H), 3.72–3.60 (m, 2H), 2.31 ppm (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=137.9, 137.5, 137.2, 131.8, 130.8, 129.5, 128.3, 128.22, 128.16, 127.82, 127.77, 127.7, 127.6, 127.4, 90.4, 88.2, 83.2, 80.2, 77.4, 77.00, 76.6, 73.1, 72.1, 71.9, 68.8, 21.0 ppm.

Synthesis of *p*-tolyl 2,3-di-*O*-benzoylthio-α-D-arabinofuranoside (25):[54] The preparation procedure is given in the Supporting Information. R_f=0.3 (EtOAc/hexane 3:7); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=8.12 (dd, J=0.6, 7.8 Hz, 2H; Ar), 8.03 (dd, J=0.6, 7.8 Hz, 2H; Ar), 7.63–7.41 (m, 8H; Ar), 7.13 (d, J=8.4 Hz, 2H; Ar), 5.72 (d, J=1.2 Hz, 2H), 5.54 (d, J=3.9 Hz, 1H), 4.58 (dd, J=3.9, 4.5 Hz, 1H), 4.03 (d, J=2.1 Hz, 1H), 2.41 (brs, 1H; O*H*), 2.32 ppm (s, 3H; CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=165.7, 165.0, 137.9, 133.4, 132.6, 129.8, 129.7, 128.8, 128.7, 128.3, 91.5 (C-1), 83.6, 81.9, 76.6, 61.7, 20.9 ppm.

Synthesis of methyl 2,3-di-*O*-benzylthio-α-D-arabinofuranoside (27):[55] The preparation procedure is given in the Supporting Information. R_f=0.4 (EtOAc/hexane 1:10); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.33–7.25 (m, 10H; Ar), 4.92 (s, 1H; H-1), 4.58–4.51 (m, 2H), 4.86–4.29 (m, 2H), 4.14–4.09 (m, 1H), 3.99–3.94 (m, 2H), 3.80–3.77 (m, 1H), 3.63–3.58 (m, 1H), 3.35 (s, 3H; OCH_3), 2.49 ppm (br, 1H; OH); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=137.4, 137.0, 128.11, 28.08, 127.6, 127.5, 107.0 (C-1), 87.6, 82.4, 82.0, 71.9, 71.5, 61.7, 54.5 ppm.

Synthesis of 2,3-di-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzoylthio-α-D-arabinofuranoside (29): A mixture of the thioarabinofuranoside **22** (1.89 g, 2.8 mmol), the thioarabinofuranosyl acceptor **25** (1 g, 2.16 mmol), and activated molecular sieves (26 g) in a dry CH_2Cl_2/CH_3CN/EtCN mixture (1:2:1, 216 mL) was stirred under N_2 from RT to −70°C for 30 min. NIS (0.63 mg, 2.8 mmol) and TMSOTf (125 μL, 0.63 mmol) were added, followed by stirring at −70°C for 0.5 h. The reaction was then quenched with Et_3N (0.1 mL), a few pieces of $Na_2S_2O_3$ (s), and satd. $NaHCO_3$ (2 mL). The mixture was stirred for 1–2 h at RT until the color of solution had changed to pale yellow, and the mixture was dried (over $MgSO_4$), filtered, and concentrated for flash chromatography over silica gel (elution: EtOAc/hexane 1: 8) to give the disaccharide **29** as a colorless oily substance (1.85 g, α/β 10:1, 85%). α-Anomer: R_f=0.4 (elution: hexane/Et_2O/CH_2Cl_2 8:1:0.4); $[\alpha]_D^{27}$=+58.1 (c=0.36 in $CHCl_3$); H NMR ($CDCl_3$, 300 MHz): δ=8.10 (d, J=7.5 Hz, 2H; Ar), 8.01 (d, J=7.2 Hz, 2H; Ar), 7.68–7.44 (m, 10H; Ar), 7.41–7.08 (m, 20H; Ar), 5.71 (d, J=0.6 Hz, 1H; H-1), 5.66–5.63 (m, 2H), 5.16 (s, 1H; H-1′), 4.71 (q, J=4.2 Hz, 1H), 4.49–4.40 (m, 4H), 4.26–4.19 (m, 1H), 4.15 (dd, J=4.5, 11.0 Hz, 1H), 4.07–4.04 (m, 2H), 3.85 (dd, J=4.2, 11.1 Hz, 1H), 3.78 (d, J=4.5 Hz, 2H), 2.29 (s, 3H; CH_3), 1.02 ppm (s, 9H; *t*Bu); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=165.4 (*C*=O), 165.3 (*C*=O), 137.91, 137.85, 137.6, 135.7, 135.6, 133.4, 132.6, 130.00, 129.9, 19.3, 129.8, 129.6, 129.2, 129.1, 128.5, 128.4, 128.3, 128.2, 127.7, 127.64, 127.61, 127.57, 127.5, 106.2 (C-1′), 91.6 (C-1), 88.4, 82.8, 82.5, 82.3, 81.7, 77.9, 71.8, 66.0, 63.6, 26.8 (C(CH_3)$_3$), 21.1 ppm (C(CH_3)$_3$); HRMS: *m/z* calcd for $C_{61}H_{62}NaO_{10}SSi$ $[M+Na]^+$: 1037.3725; found: 1037.3731 (100).

Synthesis of 2,3-di-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-α-D-arabinofuranosyl-(1→5)-1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose (30): The disaccharide **30** was prepared from the thioarabinofuranoside **22** (168 mg, 0.25 mmol) and the galactosyl acceptor **7** (50 mg, 0.19 mmol) by the LCG procedure as described for the synthesis of **29**. The crude reaction mixture (after workup) was concentrated for flash chromatography over silica gel (elution: EtOAc/hexane 1:10) to give **30** as a colorless oily substance (130 mg, α/β 10:1, 83%). α-Anomer: R_f=0.3 (EtOAc/hexane 1:6); $[\alpha]_D^{27}$=−31.2 (c=0.62 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.67–7.63 (t, J=6 Hz, 4H; Ar), 7.40–7.2 (m, 16H; Ar), 5.53 (d, J=4.8 Hz, 1H; H-1), 5.16 (s, 1H; H-1′), 4.63–4.56 (m, 2H), 4.54–4.46 (m, 3H), 4.31–4.27 (m, 2H), 4.16–4.15 (m, 1H), 4.08–4.03 (m, 3H), 3.85–3.71 (m, 4H), 1.45 (d, J=6.3 Hz, 6H; CH_3×2), 1.30 (d, J=2.4 Hz, 6H; CH_3×2), 1.03 ppm (s, 9H; *t*Bu); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=138.0, 137.7, 135.62, 135.57, 133.4, 133.3, 129.6, 128.30, 128.25, 127.7, 127.6, 127.5, 109.1 (C(CH_3)$_2$), 108.5 (C(CH_3)$_2$), 106.3 (C-1′), 96.3 (C-1), 88.0, 83.1, 82.3, 72.0, 71.6, 70.8, 70.61, 70.56, 65.6, 65.4, 63.6, 52.3, 26.8 (C(CH_3)$_3$), 26.0, 24.9, 24.5, 19.3 ppm (C(CH_3)$_3$); EI-MS: *m/z* calcd for $C_{47}H_{58}NaO_{10}Si$ $[M+Na]^+$: 833.37; found: 833.63 (100).

Synthesis of methyl 2,3-di-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (31): The disaccharide **31** was prepared from the thioarabinofuranoside **22** (255 mg, 0.38 mmol) and the thioarabinofuranosyl acceptor **27** (100 mg, 0.29 mmol) by the LCG procedure as described for the synthesis of **29**. The crude reaction mixture (after workup) was concentrated for flash chromatography over silica gel (elution: EtOAc/hexane 1:10) to give **31** as a colorless oily substance (246 mg, α/β 12:1, 95%). α-Anomer: R_f=0.2 (EtOAc/hexane 1:10); $[\alpha]_D^{27}$=+43.7 (c=0.53 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.69–7.65 (t, J=5.7 Hz, 4H; Ar), 7.41–7.19 (m, 26H; Ar), 5.16 (s, 1H; H-1′), 4.92 (s, 1H; H-1), 4.56–4.42 (m, 8H), 4.20–4.15 (m, 2H), 4.08–4.03 (m, 3H), 4.00–3.99 (m, 1H), 3.88 (dd, J=4.5, 11.5 Hz, 1H), 3.81–3.80 (d, J=4.2 Hz, 2H), 3.69 (dd, J=3.6, 11.5 Hz, 1H), 3.37 (s, 3H; CH_3), 1.04 ppm (s, 9H; *t*Bu); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=138.0, 137.9, 137.7, 137.5, 135.63, 135.58, 133.41, 129.60, 128.3, 128.29, 128.23, 127.81, 127.74, 127.60, 127.56, 127.50, 107.1 (C-1), 106.3 (C-1′), 88.3, 88.0, 83.20, 82.4, 80.6, 72.2, 71.9, 71.8, 71.7, 66, 63.6, 54.8 (CH$_3$), 26.7 (C(CH_3)$_3$), 19.2 ppm (C(CH_3)$_3$); HRMS (EI): *m/z* calcd for $C_{55}H_{62}NaO_9Si$ $[M+Na]^+$: 917.4055; found: 917.4095.

Synthesis of methyl 2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (32):[56] The disaccharide **32** was prepared from the thioarabinofuranoside **23** (199 mg, 0.378 mmol) and the thioarabinofuranosyl acceptor **27** (100 mg, 0.29 mmol) by the LCG procedure as described for the synthesis of **29**. The crude reaction mixture (after workup) was concentrated for flash chromatography over silica gel (elution: EtOAc/hexane 1:3) to give **32** as a colorless oily substance (173 mg, α/β 9:1, 80%). α-Anomer: R_f=0.5 (EtOAc/hexane 3:7); $[\alpha]_D^{27}$=+50.1 (c=1.6 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ=7.30–7.24 (m, 25H; Ar), 5.17 (s, 1H; H-1), 4.92 (s, 1H; H-1), 4.60–4.40 (m, 10H), 4.27–4.15 (m, 2H), 4.07–3.99 (m, 3H), 3.94–3.86 (m, 2H), 3.73–3.64 (m, 1H), 3.62–3.54 (m, 2H), 3.37 ppm (s, 3H; CH_3); ^{13}C NMR (75 MHz, $CDCl_3$):

δ = 137.9, 137.73, 137.70, 137.41, 137.36, 128.19, 128.16, 128.12, 127.7, 127.6, 127.55, 127.50, 127.46, 127.38, 107.0, 106.2, 88.2, 87.9, 83.3, 83.0, 80.6, 80.4, 77.4, 77.0, 76.6, 73.1, 72.1, 71.9, 71.7, 71.66, 69.4, 65.9, 54.7 ppm.

Synthesis of methyl 2,3-di-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-α-D-arabinofuranosyl-(1→5)-3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (33): The disaccharide **33** was prepared from the thioarabinofuranoside **22** (188 mg, 0.28 mmol) and the mannosyl acceptor **28** (100 mg, 0.215 mmol) by the LCG procedure as described for the synthesis of **29**. The crude reaction mixture (after workup) was concentrated for flash chromatography over silica gel (elution: EtOAc/hexane 1:8) to give **33** as a colorless oily substance (148 mg, α/β 3:1, 68%).

α-Anomer: R_f = 0.4 (EtOAc/hexane 1:4); $[\alpha]_D^{27}$ = +19.5 (c = 0.63 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.69–7.66 (m, 4H; Ar), 7.40–7.17 (m, 31H; Ar), 5.35 (s, 1H; H-1), 4.90–4.81 (m, 2H), 4.75–4.67 (m, 3H), 4.59–4.51 (m, 4H), 4.44–4.38 (m, 2H), 4.19–4.14 (m, 3H), 4.00–3.89 (m, 3H), 3.87–3.72 (m, 5H), 3.33 (s, 3H; OCH_3), 1.04 ppm (s, 9H; *t*Bu); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.3, 138.2, 137.6, 135.6, 135.59, 133.4, 129.6, 128.4, 128.28, 128.22, 128.19, 127.8, 127.76, 127.67, 127.62, 127.56, 127.5, 127.4, 107.6 (C-1′), 100.7 (C-1), 88.1, 82.6, 80.2, 80.1, 76.6, 73.6, 72.5, 71.6, 69.2, 63.6, 63.6, 26.8, 19.3 ppm; HRMS: *m/z* calcd for $C_{63}H_{70}NaO_{10}Si$ $[M+Na]^+$: 1037.4630; found: 1037.4636.

β-Anomer: R_f = 0.3 (EtOAc/hexane 1:4); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.62 (d, J = 7.5 Hz, 4H; Ar), 7.41–7.14 (m, 31H; Ar), 7.06–7.03 (m, 2H; Ar), 5.24 (d, J = 4.2 Hz, 1H; H-1), 4.84 (m, 1H), 4.78–4.75 (m, 1H), 4.70–4.67 (m, 1H), 4.61 (s, 2H), 4.53–4.44 (m, 4H), 4.33–4.19 (m, 3H), 4.13–4.06 (m, 3H), 3.98–3.77 (m, 3H), 3.69–3.67 (m, 2H), 3.62–5.59 (m, 1H), 3.52–3.47 (m, 1H), 3.31 (s, 3H; OCH_3), 1.01 ppm (s, 9H; *t*Bu); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 138.4, 138.2, 135.5, 133.4, 129.6, 128.3, 128.22, 128.17, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 99.2, 97.7, 84.4, 84.0, 82.4, 77.8, 74.7, 73.1, 72.2, 71.9, 71.6, 70.7, 69.4, 66.1, 54.9, 26.8 ($C(CH_3)_3$), 19.1 ppm ($C(CH_3)_3$).

Synthesis of methyl 2,3-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (34): The disaccharide arabinoside **31** (1.12 g, 1.25 mmol) was dissolved in THF (6.7 mL), followed by addition of Bu_4NF (0.65 g in 2.5 mL THF, 2.5 mmol). The solution was stirred at RT for 14 h and then concentrated for chromatography purification (elution: EtOAc/hexanes 3:7) to give the disaccharide **34** as a colorless oily substance (0.77 g, 94%). R_f = 0.3 (EtOAc/hexane 3:7); $[\alpha]_D^{27}$ = +57.0 (c = 1.32 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.34–7.24 (m, 20H; Ar), 5.15 (s, 1H; H-1′), 4.93 (s, 1H; H-1), 4.58–4.42 (m, 8H), 4.19–4.15 (m, 1H), 4.12–4.07 (m, 2H), 4.04 (dd, J = 6.6 Hz, 1H), 4.00–3.96 (m, 2H), 3.89–3.79 (m, 2H), 3.72–3.67 (m, 1H), 3.65–3.60 (m, 1H), 3.372 ppm (d, J = 2.1 Hz, 3H; OCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 137.7, 137.6, 137.3, 137.2, 128.19, 128.17, 128.13, 127.7, 127.66, 127.61, 127.56, 127.48, 127.46, 107.0 (C-1), 106.2 (C-1′), 88.1, 87.5, 82.9, 82.5, 81.9, 80.3, 72.0, 71.9, 71.7, 71.6, 65.7, 61.8, 54.7 ppm (OCH_3); HRMS: *m/z* calcd for $C_{39}H_{45}O_9$ $[M+H]^+$: 657.3058; found: 657.3091.

Synthesis of methyl 2,3-di-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (35)

a) By a [2+2] convergent approach (Method a in Scheme 4a): A mixture of the α-anomer of the thioarabinofuranoside **29** (185 mg, 0.18 mmol), the arabinofuranoside **34** (100 mg, 0.15 mmol), and activated molecular sieves (0.4 g) in dry CH_2Cl_2 (3.05 mL) was stirred under N_2 from RT to 0°C for 30 min. NIS (44.6 mg, 0.20 mmol) and AgOTf (11.7 mg, 0.046 mmol) were added to the mixture, followed by stirring at 0°C for 0.5 h. The reaction was then quenched with Et_3N (0.1 mL), a few pieces of $Na_2S_2O_3$ (s), and satd. $NaHCO_3$. The mixture was stirred for 1–2 h at RT and was then dried ($MgSO_4$), filtered, and concentrated for flash chromatography over silica gel (elution: EtOAc/hexane 1:4) to give **35** as a colorless oily substance (150 mg, 66%).

b) By a [2+2] convergent approach (Method b in Scheme 4a): A mixture of the α-anomer of the thioarabinofuranoside **29** (185 mg, 0.18 mmol), the arabinofuranosyl acceptor **34** (100 mg, 0.15 mmol), and activated molecular sieves (2.3 g) in dry CH_2Cl_2/CH_3CN/EtCN (1:2:1, 15.2 mL) was stirred under N_2 from RT to −40°C for 30 min. NIS (44.6 mg, 0.2 mmol) and AgOTf (11.7 mg, 0.046 mmol) were added and the mixture was stirred at −40°C. After 3 h, additional AgOTf (11.7 mg in 225 μL toluene, 0.046 mmol) was added and the system was stirred for 4 h. The reaction was then quenched by addition of Et_3N (0.1 mL), a few pieces of $Na_2S_2O_3$ (s), and satd. $NaHCO_3$. The mixture was stirred for 1–2 h at RT and was then dried ($MgSO_4$), filtered, and concentrated for flash chromatography over silica gel (elution: EtOAc/hexane 1:4) to give **33** as a colorless oily substance (196 mg, 83%).

c) By a [1+1+2] reactivity-based one-pot synthesis approach: A mixture of the thioarabinofuranosyl donor **22** (145 mg, 0.22 mmol), the thioarabinofuranosyl acceptor **25** (100 mg, 0.22 mmol), and activated molecular sieves (3.2 g) in dry CH_2Cl_2/CH_3CN/EtCN (1:2:1, 14.4 mL) was stirred from RT to −70°C under N_2 for 30 min. NIS (48.6 mg, 0.22 mmol) and TMSOTf (12.5 μL, 0.065 mmol) were added, followed by stirring at −70°C. After 0.5 h, the arabinofuranosyl acceptor **34** in dry solvent (CH_2Cl_2/CH_3CN/EtCN, 1:2:1, 7 mL) was added and the system was stirred for 10 min, followed by addition of NIS (48.6 mg, 0.22 mmol) and the increasing of the reaction temperature to −40°C. After stirring at −40°C for 1.5 h, the reaction was quenched with Et_3N (0.1 mL), a few pieces of $Na_2S_2O_3$ (s), and satd. $NaHCO_3$. The mixture was stirred for 1–2 h at RT and was then dried (over $MgSO_4$), filtered, and concentrated for flash chromatography over silica gel (elution: EtOAc/hexane 1:4) to produce **35** as a colorless oily substance (156 mg, 73% over two steps), together with trace amount of the trisaccharide **35b** (< ca. 6%).

*Data for tetrasaccharide **35***: R_f = 0.4 (EtOAc/hexane 1:3); $[\alpha]_D^{27}$ = +43.3 (c = 0.45 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.04–7.99 (m, 4H; Ar), 7.68–7.63 (m, 4H; Ar), 7.50–7.11 (m, 42H; Ar), 5.54 (d, J = 4.5 Hz, 1H), 5.51 (s, 1H), 5.31 (s, 1H; H-1″), 5.17 (s, 1H; H-1‴), 5.16 (s, 1H; H-1′), 4.91 (s, 1H; H-1), 4.58–4.46 (m, 3H), 4.06–3.99 (m, 5H), 3.96–3.88 (m, 2H), 3.85 (d, J = 4.2 Hz, 1H), 3.80–3.76 (m, 3H), 3.71–3.68 (m, 2H), 3.36 (s, 9H; OCH_3), 1.02 ppm (s, 9H; *t*Bu); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 165.2 (*C*=O), 165.1 (*C*=O), 137.8, 137.7, 137.60, 137.47, 137.38, 135.54, 135.48, 133.3, 133.14, 133.07, 129.6, 129.5, 129.1, 128.2, 127.8, 127.74, 127.68, 127.64, 127.59, 127.5, 127.4, 127.3, 107.1 (C-1), 106.2 (anomeric *C*), 106.1 (anomeric *C*), 105.6 (anomeric *C*), 88.3, 88.0, 83.1, 82.4, 82.0, 81.8, 80.5, 80.0, 72.2, 72.0, 71.9, 71.7, 66.1, 66.0, 63.6, 54.8, 26.7 ($C(CH_3)_3$), 19.1 ppm ($C(CH_3)_3$); HRMS (EI): *m/z* calcd for $C_{93}H_{98}NaO_{19}Si$ $[M+Na]^+$:1569.6364; found: 1569.6387.

*Data for trisaccharide **35b***: R_f = 0.5 (EtOAc/hexane 1:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.67–7.63 (m, 4H; Ar), 7.39–7.23 (m, 36H; Ar), 5.14 (s, 1H; H-1″), 5.13 (s, 1H; H-1′), 4.91 (s, 1H; H-1), 4.53–4.39 (m, 12H), 4.16–4.11 (m, 3H), 4.06–3.98 (m, 6H), 3.86 (dd, J = 4.2, 11.4 Hz, 2H), 3.90 (d, J = 4.2 Hz, 2H), 3.67 (dd, J = 3.3, 11.7 Hz, 2H), 3.36 (s, 9H; OCH_3), 1.03 ppm (s, 9H; *t*Bu); ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 137.9, 137.7, 137.6, 137.5, 137.38, 135.53, 135.49, 133.3, 129.5, 128.3, 128.2, 128.1, 127.8, 127.74, 127.69, 127.65, 127.54, 127.50, 127.4, 107.1 (C-1), 106.2 (anomeric *C*×2), 88.2, 87.8, 83.1, 82.3, 72.2, 71.8, 71.6, 66.0, 65.6, 63.5, 54.8, 53.3, 29.6, 26.7 ($C(CH_3)_3$), 19.2 ppm ($C(CH_3)_3$); HRMS (EI): *m/z* calcd for $C_{93}H_{98}NaO_{19}Si$ $[M+Na]^+$: 1569.6364; found: 1569.6387. EI-MS: *m/z* calcd for $C_{74}H_{82}NaO_{13}Si$ $[M+Na]^+$: 1229.54; found: 1229.67.

[2+4] convergent synthesis of methyl 2,3-di-*O*-benzyl-5-*O*-(*tert*-butyldiphenylsilyl)-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabino-furanosyl-(1→5)-2,3-di-*O*-benzoyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranosyl-(1→5)-2,3-di-*O*-benzyl-α-D-arabinofuranoside (37): A mixture of the disaccharide thioarabinoside **29** (186 mg, 0.18 mmol), the tetrasaccharide **36** (200 mg, 0.15 mmol), and activated molecular sieves (2.3 g) in dry CH_2Cl_2/CH_3CN/EtCN (1:2:1, 15.3 mL) was stirred under N_2 from RT to 0°C for 30 min. NIS (45 mg, 0.20 mmol) and TMSOTf (8.9 μL, 0.046 mmol) were added, followed by stirring at 0°C. After 1 h, the reaction was quenched with Et_3N (0.1 mL), a few pieces of $Na_2S_2O_3$ (s), and satd. $NaHCO_3$. The mixture was stirred for 1–2 h at RT and was then dried (over $MgSO_4$), filtered, and concentrated for flash chromatography over silica gel (elution: EtOAc/hexane 2:5) to produce **37** as a colorless oily substance (237 mg, 71%). R_f = 0.3 (EtOAc/hexane 2:5); $[\alpha]_D^{27}$ = +45.3 (c = 1.66 in $CHCl_3$); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.04–8.01 (m, 8H; Ar), 7.69–7.05 (m, 4H; Ar), 7.47–7.35 (m, 7H; Ar), 7.33–7.12 (m, 54H; Ar), 5.57 (m, 2H), 5.53 (m, 2H), 5.33 (m, 2H; anomeric H×2), 5.20–5.18

(m, 3H; anomeric H×2), 4.93 (s, 1H; H-1), 4.58–4.50 (m, 7H), 4.47–4.39 (m, 8H), 4.37–4.31 (m, 3H), 4.28–4.24 (m, 2H), 4.19–4.16 (m, 1H), 4.13–4.06 (m, 9H), 4.014–4.008 (m, 1H), 3.98–3.93 (m, 2H), 3.885 (dd, $J=4.5$, 12 Hz, 1H), 3.82–3.78 (m, 4H), 3.73–3.70 (m, 4H), 3.31(s, 3H; OMe), 1.03 ppm (s, 9H; *t*Bu); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta=165.39$, 165.36, 165.09, 165.05, 137.84, 137.76, 137.7, 137.6, 137.50, 137.41, 135.55, 135.49, 133.34, 133.31, 133.17, 133.12, 133.1, 133.0, 129.8, 129.47, 129.45, 129.23, 129.16, 128.3, 128.2, 128.19, 128.12, 128.07, 127.9, 127.75, 127.72, 127.69, 127.65, 127.59, 127.51, 127.47, 127.42, 127.329, 107.109 (C-1), 106.3 (anomeric C), 106.13 (anomeric C), 106.07 (anomeric C), 105.7 (anomeric C), 105.6 (anomeric C), 88.5, 88.31, 88.28, 88.07, 83.10, 82.7, 82.4, 82.0, 81.99, 81.86, 81.81, 80.5, 80.04, 79.98, 77.5, 77.4, 77.3, 77.0, 76.8, 72.2, 72.0, 71.9, 71.83, 71.82, 71.77, 71.6, 66.1, 66.0, 65.9, 65.8, 63.5, 54.8, 52.2, 26.7, 19.2 ppm; HRMS: *m/z* calcd for $C_{131}H_{134}KO_{29}Si$ $[M+K]^+$: 2237.8412; found: 2237.8412.

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[30] The yield for oxazoline **18** was improved from 40 to 70% during the revision period of this manuscript, but we have not yet applied such a modified procedure to the preparation of **17** and **19**. The modified procedure applied the sonication to accerelate the reductive removal of iodine and the detail was given in the Experimental Section.
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